

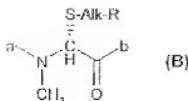
AMENDMENTS TO THE CLAIMSCLAIMS

1. (original) Use of a non-immunosuppressive, cyclophilin-binding cyclosporin in the manufacture of a medicament for treating or preventing ischemic brain damage, traumatic brain or spinal cord injury or stroke.
2. (original) A method for the treatment or the prevention of ischemic brain damage or traumatic brain or spinal cord injury in a patient suffering from or at risk of suffering from such a disease or condition, comprising administering to said patient an effective amount of a non-immunosuppressive, cyclophilin-binding cyclosporin.

3. (currently amended) A use according to Claim 1 or a method according to Claim 2, in which the non-immunosuppressive, cyclophilin-binding cyclosporin is a compound of formula (A):

-MeBmt- α -Abu-B-C-Val-MeLeu-Ala-(D)Ala-MeLeu-MeLeu-MeVal-
1 2 3 4 5 6 7 8 9 10 11 (A)

wherein B is an amino acid residue of formula (B):



wherein

a denotes the bond to the α -Abu residue in position 2;

b denotes the bond to the residue C in the 4 position;

Alk represents straight-or branched-chain alkylene containing from 2-6 carbon atoms or cycloalkylene containing from 3-6 carbon atoms; and

R represents

a carboxy or alkyloxycarbonyl radical;

a radical-NR₁R₂,

in which

R₁ and R₂ are the same or different and represent hydrogen, alkyl, C₂₋₄alkenyl,

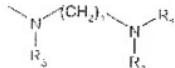
C₃₋₆cycloalkyl, phenyl (optionally substituted by halogen, alkoxy,

alkoxycarbonyl, amino, alkylamino or dialkylamino) or a benzyl or saturated or

unsaturated heterocycll radical containing 5- or 6-ring atoms and 1-3 heteroatoms, or

R₁ and R₂ form, together with the nitrogen atom to which they are attached, a saturated or unsaturated heterocycle containing 4-6 ring atoms and optionally containing a further heteroatom selected from nitrogen, oxygen or sulphur and optionally substituted by alkyl, phenyl or benzyl;

a radical of formula:



wherein

R₁ and R₂ are as defined above;

R₃ represents hydrogen or an alkyl radical; and

n is a whole number from 2-4; and

alkyl denotes straight-or branched-chain alkyl containing from 1-4 carbon atoms;

C is MeLeu or 4-hydroxy-MeLeu;

and the pharmaceutically acceptable salts thereof.

4. (currently amended) A use according to Claim 1 or a method according to Claim 2, in which the non immunosuppressive, cyclophilin-binding cyclosporin is a compound of formula (I):

- W - X - R - Y - Z - Q - Ala - (D)Ala - MeLeu - MeLeu - MeVal -
1 2 3 4 5 6 7 8 9 10 11 (I)

in which

W is MeBmt, dihydro-MeBmt or 8'-hydroxy-MeBmt;

X is αAbu, Val, Thr, Nva or O-methyl threonine (MeOThr);

R is Sar or (D)-MeAla;

Y is MeLeu, γ-hydroxy-MeLeu, Melle, MeVal, MeThr, MeAla, Me Tyr, MeTyr(O-PO(OH)₂), Mealle or MeaThr or Pro;

Z is Val, Leu, N-Alk-Val or N-Alk-Leu, wherein Alk represents Me or Me substituted by vinyl optionally substituted by phenyl, or an N, S or O heteroaryl containing 6 ring members, or phenyl optionally substituted by halogen; and

Q is MeLeu, γ-hydroxy-MeLeu or MeAla.

5. (currently amended) A use according to Claim 1 or a method according to Claim 2, in which the non-immunosuppressive, cyclophilin-binding cyclosporin is a compound selected from the group comprising:

- a) [dihydro-MeBmt]-[γ -hydroxy-MeLeu]⁴-Ciclosporin;
- b) [MeVal]⁴-Ciclosporin;
- c) [Melle]⁴-Ciclosporin;
- d) [MeThr]⁴-Ciclosporin;
- e) [γ -hydroxy-MeLeu]⁴-Ciclosporin;
- f) [Nva]²-[γ -hydroxy-MeLeu]⁴-Ciclosporin;
- g) [γ -hydroxy-MeLeu]⁴-[γ -hydroxy-MeLeu]⁶-Ciclosporin;
- h) [MeVal]⁵-Ciclosporin;
- i) [MeOThr]²-[(D)MeAla]³-[MeVal]⁵-Ciclosporin;
- j) [8'-hydroxy-MeBmt]¹-Ciclosporin;
- k) [MeAla]⁶-Ciclosporin;
- l) [DMeAla]³-[MeTyr(OPO(OH)₂)]⁴-Ciclosporin;
- m) [N-Benzyl-Val]⁵-Ciclosporin;
- n) [N-5-Fluoro-Benzyl-Val]⁵-Ciclosporin;
- o) [N-Allyl-Val]⁵-Ciclosporin;
- p) [N-3-Phenyl-Allyl-Val]⁵-Ciclosporin;
- q) [Pro]⁴-Ciclosporin or
- r) [γ -hydroxy-MeLeu]⁹-Ciclosporin.

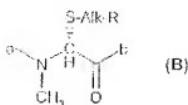
6. (currently amended) A use according to Claim 1 or a method according to Claim 2, in which the non-immunosuppressive, cyclophilin-binding cyclosporin is [Melle]⁴-Ciclosporin or [γ -hydroxy-MeLeu]⁴-Ciclosporin.

7. (new) A use according to Claim 2, in which the non-immunosuppressive, cyclophilin-binding cyclosporin is a compound of formula (A):

-MeBmt- α Abu-B-C-Val-MeLeu-Ala-(D)Ala-MeLeu-MeLeu-MeVal-

1 2 3 4 5 6 7 8 9 10 11 (A)

wherein B is an amino acid residue of formula (B):



wherein

a denotes the bond to the α Abu residue in position 2;

b denotes the bond to the residue C in the 4 position;

Alk represents straight-or branched-chain alkylene containing from 2-6 carbon atoms or cycloalkylene containing from 3-6 carbon atoms; and

R represents

a carboxy or alkoxy carbonyl radical;

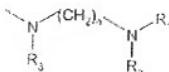
a radical-NR₁R₂,

in which

R₁ and R₂ are the same or different and represent hydrogen, alkyl, C₂₋₄alkenyl, C₃₋₆cycloalkyl, phenyl (optionally substituted by halogen, alkoxy, alkoxy carbonyl, amino, alkylamino or dialkylamino) or a benzyl or saturated or unsaturated heterocycl radical containing 5- or 6-ring atoms and 1-3 heteroatoms, or

R₁ and R₂ form, together with the nitrogen atom to which they are attached, a saturated or unsaturated heterocycle containing 4-6 ring atoms and optionally containing a further heteroatom selected from nitrogen, oxygen or sulphur and optionally substituted by alkyl, phenyl or benzyl;

a radical of formula:



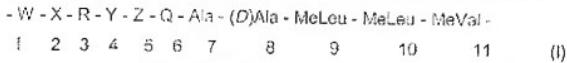
wherein

R₁ and R₂ are as defined above;

R₃ represents hydrogen or an alkyl radical; and

n is a whole number from 2-4; and
 alkyl denotes straight-or branched-chain alkyl containing from 1-4 carbon atoms;
 C is MeLeu or 4-hydroxy-MeLeu;
 and the pharmaceutically acceptable salts thereof.

A use according to Claim 1 or a method according to Claim 2, in which the non-immunosuppressive, cyclophilin-binding cyclosporin is a compound of formula (I):



in which

W is MeBmt, dihydro-MeBmt or 8'-hydroxy-MeBmt;

X is α Abu, Val, Thr, Nva or O-methyl threonine (MeOThr);

R is Sar or (D)-MeAla;

Y is MeLeu, γ -hydroxy-MeLeu, Melle, MeVal, MeThr, MeAla, Me Tyr, MeTyr(O-PO(OH)₂), Mealle or MeaThr or Pro;

Z is Val, Leu, N-Alk-Val or N-Alk-Leu, wherein Alk represents Me or Me substituted by vinyl optionally substituted by phenyl, or an N, S or O heteroaryl containing 6 ring members, or phenyl optionally substituted by halogen; and

Q is MeLeu, γ -hydroxy-MeLeu or MeAla.

8. (new) A use according to Claim 2, in which the non-immunosuppressive, cyclophilin-binding cyclosporin is a compound selected from the group comprising:

- a) [dihydro-MeBmt]-[γ -hydroxy-MeLeu]⁴-Ciclosporin;
- b) [MeVal]⁴-Ciclosporin;
- c) [Melle]⁴-Ciclosporin;
- d) [MeThr]⁴-Ciclosporin;
- e) [γ -hydroxy-MeLeu]⁴-Ciclosporin;
- f) [Nva]²-[γ -hydroxy-MeLeu]⁴-Ciclosporin;
- g) [γ -hydroxy-MeLeu]⁴-[γ -hydroxy-MeLeu]⁶-Ciclosporin;
- h) [MeVal]⁵-Ciclosporin;

i) [MeOThr]²-[(D)MeAla]³-[MeVal]⁵-Ciclosporin;

j) [8'-hydroxy-MeBmt]¹-Ciclosporin;

k) [MeAla]⁶-Ciclosporin;

l) [DMeAla]³-[MeTyr(OPO(OH)₂)₂]⁴-Ciclosporin;

m) [N-Benzyl-Val]⁵-Ciclosporin;

n) [N-5-Fluoro-Benzyl-Val]⁵-Ciclosporin;

o) [N-Allyl-Val]⁵-Ciclosporin;

p) [N-3-Phenyl-Allyl-Val]⁵-Ciclosporin;

q) [Pro]⁴-Ciclosporin or

r) [γ -hydroxy-MeLeu]⁹-Ciclosporin.

9. (new) A use according to Claim 2, in which the non-immunosuppressive, cyclophilin-binding cyclosporin is [Melle]⁴-Ciclosporin or [γ -hydroxy-MeLeu]⁴-Ciclosporin.